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Electrophysiological analysis of oscillatory networks supporting human memory maintenance

PhD booklet thesis

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GENERAL BACKGROUND AND AIM OF THE THESIS

Short-term memory (STM) refers to the ability to transiently maintain information in memory when it is no longer present in the environment, till the behavior is accomplished. During ontogenesis, this ability shows a specific decline as a function of advancing age. It is still largely unknown which neurophysiological mechanisms contribute to the efficient maintenance of representations. In the present thesis, I hope to conduce to our limited knowledge on this topic by discussing two studies, both investigating the functional connectivity networks underlying short-term memory maintenance and their relation to cognitive aging. In both studies, the significance of functional connectivity in STM was tested by the assessment of phase synchronization within theta oscillation (4-8 Hz) between the fronto-midline (FM) cortex and the rest of the brain. A visual delayed match-to-sample task was applied for the investigation of the processes distinctive of short term maintenance. In this conventionally used STM paradigm, participants are presented with a set of visual items sequentially or simultaneously and are instructed to maintain their memory in mind over an interval of seconds (delay period) after the stimuli is no longer present. Following the delay period, a single probe item or array is presented and participants indicate whether the probe matches the item(s) of the previous stimuli. By the application of this paradigm, memory maintenance delay periods associated with subsequent correct recognition could be separated from item maintenance periods associated with failure of recognition, providing us with an opportunity to contrast the functional connectivity correlates of subsequent memory effects. In the first study, we focused on memory maintenance related functional connectivity in relation with subsequent memory effects, memory demands and cognitive aging. The second study presented here aimed to provide evidence for the notion that memory maintenance related functional connectivity of frontal theta oscillations contribute both to efficient STM performance and encoding to long term episodic memory.

RESEARCH QUESTION OF THE THESIS

STUDY 1

In the first study, the functional connectivity of FM theta oscillation in relation to memory maintenance processes was investigated in a young and in an elderly population. The main research questions and the corresponding results were the following:

1) It was hypothesized that phase synchronization of the theta rhythm mediates active maintenance of information rather than reflect general sustained attention during a cognitive task. Therefore it was tested whether large-scale theta connectivity of the midline frontal cortex and other brain areas was facilitated during the maintenance of information compared to a sustained attention-demanding perceptual oddball task. As a result, substantially stronger connectivity was observed within the FM cortex and between the FM and lateral frontal and temporal regions during the retention period of the STM task compared to that seen in the control perceptual task.

2) It was hypothesized that if temporary retention of information is mediated by the increased functional connectivity of frontal cortex, that should also be predictive for the efficiency of these processes. Therefore it was tested for the first time whether connectivity patterns of the FM theta band activity during the delay period of a STM task were directly related to STM recognition performance. Subsequent STM memory effect was expected, meaning that the interregional connectivity strength during memory maintenance period would be higher for the later remembered items compared to connectivity measures related to forgotten stimuli. According to our results, FM-temporal and FM-occipital interactions were substantially stronger during the successfully maintained, i.e. later correctly recognized trials within and between the

frontal cortices. The present data support the hypothesis that theta activity in the delay period is predictive for the efficiency of memory performance.

3) It was hypothesized that additional processes may be required for efficient retention compared to those related to storage demands. Therefore it was tested whether the functional connectivity of theta oscillation related to subsequent memory effects, and that related to memory load showed different or identical patterns. Increased interaction was shown in the theta band functional network between FM and visual cortices (occipital regions) and also between FM sites and higher-order sensory areas of the parietal region as an effect of increasing memory load. According to our findings, the couplings within the region of the frontal cortex and between fronto-temporal sites were not sensitive to the modulation of memory load, but were predictive for the efficiency of maintenance processes. Thus, it appears that fronto-parietal connectivity corresponds to the amount of information to be held in working memory (WM) even if item recognition fails. This result indicates that the process of effective active maintenance is at least distinguishable from the actual capacity of WM retention.

4) It was hypothesized that the decline of frontal brain functions of normal aging may affect maintenance of information thereby leading to impaired performance on a delayed matching-to-sample task (DMST). In order to test this, we investigated whether the effect of cognitive aging on memory maintenance processes was mediated by the disconnection of the functional networks in theta band. In the elderly, reduced performance was associated with an observed decline of connectivity strength within the FM and between FM - lateral-frontal and FM-temporal regions. These age-related differences were found to be absent in the control task and were only evident during the delay period of the DMST task, indicating that active memory maintenance is specifically affected by advancing age. This result suggests that the disconnection of frontal cortex may lead to deficits of the active maintenance process.

5) It was hypothesized that the phase synchronization of frontal cortex in theta band predicts individual differences of short term memory performance and working memory capacity. Significant positive correlations were observed between the individual connectivity strength (within FM and between FM and all lobes of the brain) and memory performance. The individual WM capacity measured by digit span task was predicted by the strength of fronto-parietal and fronto-occipital connectivity.

STUDY 2

The second study was aimed to investigate the interaction of short term memory maintenance processes with operations that contribute to the formation of long term memory representations. The main hypotheses and corresponding results were the following:

1) It was hypothesized that during the DMST using unique complex visual stimuli initiate not just temporary retention of information but also lead to incidental episodic memory formation. Therefore the memory performance was tested following a temporary retention period and also after an hour during an unexpected later test. According to our findings, memory performance during long term memory tests were high above the chance level which indicates that even though the task required keeping in mind the memoranda only for a few seconds the memory recognition judgments were based upon efficiently formed short and then long lasting representations of the stimuli.

2) It was hypothesized that the neurophysiological processes that help the system to keep information in STM during the delay period of a DMST task also enable long-term memory formation, and therefore the systems of STM and LTM may share common processes that operate on them. Therefore it was tested if the phase synchronization strength during the delay period of a DMST positively correlated with the subsequent long term memory performance. It

was found that EEG theta phase synchronization during the period of STM maintenance particularly between the fronto-midline and middle temporal, parahippocampal regions was correlated with subsequent successful LTM recognition, substantiating the claim that theta oscillations modulate successful LTM formation.

3) It was hypothesized that the phase synchronization of theta oscillation, particularly between the frontal and the midline temporal, parahippocampal regions, was involved in the delay period of a DMTS task. Therefore it was tested if large-scale theta connectivity of frontal cortices and the middle temporal brain areas was facilitated during the maintenance of information compared to resting state. The contrast of retention periods of a DMST with the control resting state permitted the assessment of the theta functional connectivity network of frontal and anterior cingular cortices related to efficient memory processes (only trials associated with correct recognition were entered into the analysis). Memory maintenance operations were found to involve distributed neural networks across multiple brain regions. Substantially stronger memory related connectivity of the midline frontal gyrus and the inferior frontal gyrus was evident and most of these interactions involved the entire temporal lobe, the dorsal and ventral visual streams and visual association cortices such as the superior parietal gyrus.

4) It was hypothesized that the connectivity network of frontal cortical regions related to STM and LTM may not entirely overlap but may become dissociated. We looked at the functional connectivity differences between the trials in which recognition was correct both in the STM and LTM tests and the trials in which recognition was correct only in the STM test. Most of the functional connections forming the delay period network did not show differences between the trials in which recognition was correct in LTM test relative to the trials associated only STM recognition. This interesting finding further supports the claim of overlapping mechanisms in both memory systems.

GENERAL DISCUSSION

The active maintenance process keeps information in a highly activated state, thus making it available for further cognitive action and protecting it from decay. Based on the results, we conclude that the functional interactions of the frontal cortex as realized by theta oscillatory patterns may act as a control mechanism that provides repetitive refreshment for the neuronal representations of the memoranda. A possible function of theta oscillation therefore is to enable a sustained neural activation that can bridge the temporal gap of the delay period between stimulus presentation and memory testing. However, it is well-established that the amplitude of this oscillation decreases over time in the lack of regular refreshment. This hypothesis suggests that the content of memory will decay if frontal theta connectivity fails to reach an optimal level for its updating. This mechanism implies that theta activity modulated by the frontal cortices might enhance neural representations of relevant sensory stimuli by controlling when and which representations are reactivated in the sensory and temporal cortices, thereby protecting information from decay. The above mechanism is supported by models suggesting that the top-down signals from the frontal cortex select and reactivate temporarily stored representations thus enhancing the rehearsal of those items. The observation, that in the elderly reduced connectivity strength of FM theta is associated with decreased performance, implicates that the postulated FM theta related mechanism of active maintenance process is especially vulnerable to aging.

Although short term and long-term memory have traditionally been considered as separate systems, both are supported by phase synchronization of theta oscillation, particularly by functional interplay between frontal cortices and temporal brain regions. According to Hebb's proposal (Hebb, 1949), sustained activation in STM networks is maintained by reverberating activity in neuronal assemblies. Consequently, based on presented empirical data, synchronized oscillatory activity may coordinate activity in the network of distributed areas and may also establish reverberating activity in the system. Thus, we propose that processes associated with STM - particularly the maintenance of representations - support LTM formation through

synchronization-based mechanisms and therefore the systems of STM and LTM may share common processes that operate on them. Taken together the current stage of knowledge in contrary to the assumptions suggested by the multi-store model of STM implies that it is unlikely that STM and LTM would be fully separable systems on a neurophysiological level since the medial-temporal lobe (MTL) is also engaged in STM tasks and not just uniquely during LTM formation. Additionally the prefrontal cortices are not likely to be the storage buffer of the STM content, but rather serve as a control of attention allocation on items stored in the sensory brain regions. In conclusion the present findings support the unitary store models of STM.

List of publications related to this summary:

Tóth, B., Kardos, Z., File, B., Boha, R., Stam, C. J., & Molnár, M. (2014). Frontal midline theta connectivity is related to efficiency of WM maintenance and is affected by aging. Neurobiology of learning and memory, 114C, 58–69.

Kardos, Z., Tóth, B., Boha, R., File, B., & Molnár, M. (2014). Age-related changes of frontal-midline theta is predictive of efficient memory maintenance. Neuroscience, 273, 152–162.

Tóth, B., File, B., Boha, R., Kardos, Z., Hidasi, Z., Anna, Z., & Csibri, É. (2014). EEG network connectivity changes in mild cognitive impairment — Preliminary results. International Journal of psychophysiology 92 1-7

Tóth, B., Boha, R., Posfai , M., Gaál, Zs. A., Kónya, A., Stam, C. J., Molnár, M. (2012) EEG synchronization characteristics of functional connectivity and complex network properties of memory maintenance in the delta and theta frequency bands; International Journal of Psychophysiology 83: (3) pp. 399-402.